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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
05/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,785	NONOMURA ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/04/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 03/10/10 are acknowledged.

2. Claims 1-22 were cancelled.

3. New claim 32 was added.

4. Claims 23-32 are included in the prosecution.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 05/04/10 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement.

See attached copy of PTO-1449.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 23-31 **remain** rejected and **new claim 32** is rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al. (WO 02/44167).

The claimed invention is a process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active

isomer (R-isomer) of lansoprazole at about 20 to about 100°C for a time sufficient to produce the amorphous optically active isomer of lansoprazole.

Hashimoto teaches a method of producing (R)-lansoprazole (Abstract). The (R) -lansoprazole produced by the method may be a solid (crystal or amorphous) form of (R)-lansoprazole and may be a hydrate. “The "hydrate” includes 0.5 hydrate to 5.0 hydrate. More preferred is 0.5 hydrate, 1.0 hydrate and 1.5 hydrate” (Page 8, lines 15-23). “The thus-obtained crystal may be used as it is, or dried … The "drying" includes, for example, vacuum drying, through-flow drying, drying by heating, air drying and the like” (Page 14, lines 1-5).

Hashimoto does not expressly teach the process of drying the hydrate of (R)-lansoprazole in the temperature range of about 20 to about 100°C.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because during the process of routine experimentation one would store the (R)-lansoprazole at room temperature or would dry the (R)-lansoprazole, which would lead to the formation of an amorphous (R)-lansoprazole.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed

invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 23, the process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C would have been obvious over the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 8, lines 15-23 and Page 14, lines 1-5).

Regarding instant claim 24, the limitation of heating at about 40 to about 80°C would have been obvious over the method of drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 14, lines 1-5). One with ordinary skill in the art would modify the storage or drying temperature of a hydrate of (R)-lansoprazole during the process of routine experimentation and the recited temperature range would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claim 25, the limitation of 0.5 to 1.5 hydrate crystals of (R)-lansoprazole would have been obvious over the 0.5 hydrate, 1.0 hydrate and 1.5 hydrate taught by Hashimoto (Page 8, lines 15-23).

Regarding instant claim 26, the limitation of the keeping of the temperature under reduced pressure or under ventilation would have been obvious over the vacuum drying, through-flow drying, drying by heating, and air drying taught by Hashimoto (Page 14, lines 1-5).

Regarding instant claim 27, the limitation of the amorphous optically active isomer of lansoprazole that does not show a specific peak under an X-ray powder diffraction analysis would have been obvious over the amorphous lansoprazole isomer taught by Hashimoto (Page 8, lines 15-17). One of ordinary skill in the art would find analyzing the resultant lansoprazole isomer under X-ray powder diffraction obvious. Since the amorphous lansoprazole isomer is rendered obvious by Hashimoto, the property associated with the amorphous lansoprazole isomer (i.e., not showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Regarding instant claims 28-29, the limitation of the hydrated crystals that show a specific peak under an X-ray powder diffraction analysis would have been obvious over the hydrated crystals taught by Hashimoto (Page 8, lines 18-19). One of ordinary skill in the art would find analyzing the resultant hydrated crystal of (R)-lansoprazole under X-ray powder diffraction obvious. Since the hydrated crystal of (R)-lansoprazole is rendered obvious by Hashimoto, the property associated with the hydrated crystal of (R)-lansoprazole (i.e., showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. The limitation of drying the hydrated crystals at about 60ºC-70ºC

would have been obvious over the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 8, lines 15-23 and Page 14, lines 1-5).

Regarding instant claims 30-31, the limitation of the amorphous optically active isomer of lansoprazole that contains more amorphous form than crystalline form would have been obvious over the amorphous (R)-lansoprazole and the hydrated crystal of (R)-lansoprazole taught by Hashimoto (Page 8, lines 15-23 and Page 14, lines 1-5). One of ordinary skill in the art would find it obvious to modify the drying steps to increase crystalline lansoprazole or increase the amorphous lansoprazole formation.

Regarding **new claim 32**, the limitation of the amorphous optically active isomer of lansoprazole that is unstable to atmospheric moisture and in acids would have been obvious over the amorphous form of (R)-lansoprazole taught by Hashimoto (Page 8, lines 15-23). Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. Since Hashimoto teaches amorphous (R)-lansoprazole, the properties associated with the amorphous (R)-lansoprazole (such as instability to atmospheric moisture and acid) are necessarily present.

Response to Arguments

8. Applicant's arguments, see Page 4, filed 03/10/10, with respect to the rejection of claims 23-31 under 35 USC § 103(a) as being unpatentable over Hashimoto et al. (WO 02/44167) have been fully considered but are not persuasive.

Applicant argues that "at the time the invention was made, the amorphous phase of the active pharmaceutical ingredient (API) was avoided in general." Applicant points to the Brodka-Pfeiffer et al. and the Bauer references and argues that "… amorphous APIs are usually unstable, and tend to convert to the stable, crystalline state. This reaction – when it occurs in a pharmaceutical preparation – is frequently regarded as undesirable because the amorphous drug particles may have an adverse effect on the properties of the solid phase preparation during storage … Thus, in the field of pharmaceutical preparations, the amorphous state of the API was generally avoided." Applicant argues that when Hashimoto is understood as a whole, it is clear that none of the steps discussed at page 8, lines 15-23 and page 14, lines 1-5 correspond to the step of claim 23. Applicant argues that when Hashimoto is understood as a whole, it is clear that the dried product of the "thus-obtained crystal" described on page 14, lines 1-5 is a crystal exhibiting specific peaks under X-ray powder diffraction analysis. Applicant argues that "… given that there was sparse information on appropriate handling of amorphous solids with the aim of achieving a thermodynamically stable product, the present record provides no basis to conclude that there would have been a reasonable expectation of success in achieving the features of claim 23."

This is not persuasive because Hashimoto teaches that the (R)-lansoprazole produced is amorphous (Page 8, lines 15-23). Hashimoto also teaches that a crystal of (R)-lansoprazole that may be a hydrate is produced (Page 3, lines 15-23) and that the crystal that is obtained may be dried by vacuum drying, through-flow drying, drying by heating, air drying etc. (Page 14, lines 1-5). Therefore, the claimed elements of the

process of producing an amorphous optically active isomer of lansoprazole are disclosed by Hashimoto and one of ordinary skill in the art would perform the drying step (of the hydrate) at various temperature ranges during the process of routine experimentation with a reasonable expectation of producing an amorphous optically active isomer of lansoprazole.

Therefore, the rejection of 11/10/09 is maintained.

Claim Rejections - 35 USC § 103

9. Claims 23-31 **remain** rejected and **new claim 32** is rejected under 35 U.S.C. 103(a) as being unpatentable over Fujishima et al. (WO 00/78745).

Fujishima teaches isolation of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole (R(+)-lansoprazole) where the filtrate was evaporated to dryness to yield R(+)-lansoprazole as an amorphous substance (Page 13, line 30 to Page 14, line 16). The starting material is a crystal of R(+)-lansoprazole which may be a hydrate (Page 2, lines 32-34). The hydrate may be a 0.5 hydrate to 5.0 hydrate (Page 2, line 35 to Page 3, line 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of evaporating a hydrate of R(+)-lansoprazole to dryness, as taught by Fujishima, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because during the process of routine experimentation one would store the (R)-lansoprazole at

room temperature or would dry the (R)-lansoprazole, which would lead to the formation of an amorphous (R)-lansoprazole.

Regarding instant claim 23, the process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C would have been obvious over the method of evaporating to dryness a hydrate of R(+)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16, Page 2, lines 32-34).

Regarding instant claim 24, the limitation of heating at about 40 to about 80°C would have been obvious over the method of evaporating to dryness a hydrate of R(+)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16). One with ordinary skill in the art would modify the storage or drying temperature of a hydrate of (R)-lansoprazole during the process of routine experimentation and the recited temperature range would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claim 25, the limitation of 0.5 to 1.5 hydrate crystals of (R)-lansoprazole would have been obvious over the 0.5 hydrate, 1.0 hydrate and 1.5 hydrate taught by Fujishima (Page 2, line 35 to Page 3, line 3).

Regarding instant claim 26, the limitation of the keeping of the temperature under reduced pressure or under ventilation would have been obvious over the evaporating to dryness taught by Fujishima (Page 13, line 30 to Page 14, line 16). One of ordinary skill in the art would use the available methods of drying during the process of routine

experimentation, including evaporation or air drying, drying by increasing the temperature, and maintaining the temperature under reduced pressure.

Regarding instant claim 27, the limitation of the amorphous optically active isomer of lansoprazole that does not show a specific peak under an X-ray powder diffraction analysis would have been obvious over the amorphous lansoprazole isomer taught by Fujishima (Page 13, line 30 to Page 14, line 16). One of ordinary skill in the art would find analyzing the resultant lansoprazole isomer under X-ray powder diffraction obvious. Since the amorphous lansoprazole isomer is rendered obvious by Fujishima, the property associated with the amorphous lansoprazole isomer (i.e., not showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Regarding instant claims 28-29, the limitation of the hydrated crystals that show a specific peak under an X-ray powder diffraction analysis would have been obvious over the method of evaporating to dryness a hydrate of R(+)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16, Page 2, lines 32-34). One of ordinary skill in the art would find analyzing the resultant hydrated crystal of (R)-lansoprazole under X-ray powder diffraction obvious. Since the hydrated crystal of (R)-lansoprazole is rendered obvious by Fujishima, the property associated with the hydrated crystal of (R)-lansoprazole (i.e., showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its

properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. The limitation of drying the hydrated crystals at about 60ºC-70 ºC would have been obvious over the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16, Page 2, lines 32-34).

Regarding instant claims 30-31, the limitation of the amorphous optically active isomer of lansoprazole that contains more amorphous form than crystalline form would have been obvious over the amorphous (R)-lansoprazole and the hydrated crystal of (R)-lansoprazole taught by Fujishima (Page 13, line 30 to Page 14, line 16 and Page 2, lines 32-34). One of ordinary skill in the art would find it obvious to modify the drying steps to increase crystalline lansoprazole or increase the amorphous lansoprazole formation.

Regarding **new claim 32**, the limitation of the amorphous optically active isomer of lansoprazole that is unstable to atmospheric moisture and in acids would have been obvious over the (R(+)-lansoprazole) in an amorphous form as taught by Fujishima (Page 13, line 30 to Page 14, line 16). Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. Since Fujishima teaches amorphous R(+)-lansoprazole, the properties associated with the amorphous R(+)-lansoprazole (such as instability to atmospheric moisture and acid) are necessarily present.

Response to Arguments

10. Applicant's arguments, see Page 6, filed 08/24/09, with respect to the rejection of claims 23-31 under 35 USC § 103(a) as being unpatentable over Fujishima et al. (WO 00/78745) have been fully considered but are not persuasive.

Applicant argues that when Fujishima is considered as a whole and in view of the general understanding of the amorphous phase in pharmaceutical solids at the time the invention was made, there would not have been a reasonable expectation of success in producing an amorphous optically active isomer of lansoprazole from hydrated crystals of optically active isomer (R-isomer) of lansoprazole by routine experimentation. Applicant argues that "given that there was sparse information on appropriate handling of amorphous solids with the aim of achieving a thermodynamically stable product, it is clear that Fujishima fails to provide any basis to show that there would have been a reasonable expectation of success in achieving the features of claim 23." Applicant argues that when Fujishima is understood as a whole, it is clear that none of the steps discussed at page 13, line 30 to page 14, line 16 and page 2, line 32 to page 3, line 3 correspond to the step of claim 23.

This is not persuasive because Fujishima teaches the claimed elements of the process of the isolation of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-I H-benzimidazole (R(+)-lansoprazole) where the filtrate was evaporated to dryness to yield R(+)-lansoprazole as an amorphous substance (Page 13, line 30 to Page 14, line 16). Fujishima also teaches that the starting material is a crystal of R(+)-lansoprazole which may be a hydrate (a 0.5 hydrate to 5.0 hydrate)

(Page 2, line 32 to Page 3, line 3). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of evaporating a hydrate of R(+)-lansoprazole to dryness, as taught by Fujishima, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention. One of ordinary skill in the art would find it obvious to use the amorphous optically active R(+)-lansoprazole since this material would necessarily be produced after following the process of Fujishima, the general state of the art regarding the amorphous phase of pharmaceutical solids notwithstanding.

Therefore, the rejection of 11/10/09 is maintained.

Conclusion

11. No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Humera N. Sheikh/
Primary Examiner, Art Unit 1615